ENVIRONMENTAL TOBACCO SMOKE*

First Listed in the *Ninth Report on Carcinogens*

CARCINOGENECITY

Environmental tobacco smoke (ETS) is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans that indicate a causal relationship between passive exposure to tobacco smoke and human lung cancer (reviewed in IARC V. 38 1986; US EPA 1992, CEPA 1997). Studies also support an association of ETS with cancers of the nasal sinus (CEPA 1997).

Evidence for an increased cancer risk from ETS is from studies examining nonsmoking spouses living with individuals who smoke cigarettes, exposures of nonsmokers to ETS in occupational settings, and exposure to parents' smoking during childhood. Many studies, including recent large population-based case control studies, have demonstrated increased risks of about 20% for developing lung cancer following prolonged exposure to ETS, with some studies suggesting higher risks with higher exposures. Exposure to ETS from spouses smoking or exposure in an occupational setting appears most strongly related to increased risk.

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

ETS is a complex mixture of gases and particles comprising smoke from the burning cigarette, cigar or pipe tip (sidestream smoke), mainstream smoke which is not inhaled by the smoker, and exhaled smoke. Sidestream smoke and mainstream smoke contain many of the same chemical constituents including at least 250 chemicals known to be toxic or carcinogenic. There is evidence from animal studies that the condensate of sidestream smoke is more carcinogenic to the skin of mice than equivalent weight amounts of mainstream smoke. Exposure to primarily mainstream smoke through active tobacco smoking has been determined to cause cancer of the lung, urinary bladder and renal pelvis, oral cavity, pharynx, larynx, esophagus, lip, and pancreas in humans. Between 80 to 90% of all human lung cancers are attributed to tobacco smoking.

Exposure of nonsmokers to ETS has been demonstrated by detecting nicotine, respirable smoke particulates, tobacco specific nitrosamines and other smoke constituents in the breathing zone, and by measurements of a nicotine metabolite (cotinine) in the urine. However, there is no good biomarker of cumulative past exposure to tobacco smoke, and all of the information collected in epidemiology studies determining past exposure to ETS relies on estimates which may vary in their accuracy (recall bias). Other suggestions of systematic bias have been made concerning the epidemiological information published on the association of ETS with cancer. These include misclassification of smokers as nonsmokers, factors related to lifestyle, diet, and other exposures that may be common to couples living together and that may influence lung cancer incidence, misdiagnosis of metastatic cancers from other organs in the lung, and the possibility that epidemiology studies examining small populations and showing no effects of ETS would not be published (publication bias).

---

* There is no separate CAS registry number assigned to environmental tobacco smoke.

Three recent population-based (Stockwell *et al.* 1992; Brownson *et al*. 1992; Fontham *et al.* 1994) and one hospital-based (Kabat *et al*. 1995) case control studies have addressed potential systematic biases. The three population-based studies each showed an increased risk from prolonged ETS exposure of a magnitude consistent with prior estimates. The hospital-based study gave similarly increased risk estimates, but the results were not statistically significant. The potential for publication bias has been examined and dismissed (CEPA 1997), and the reported absence of increased risk for lung cancer for nonsmokers exposed only in occupational settings has been found not to be the case when the analysis is restricted to higher quality studies (Wells 1998). Thus, factors related to chance, bias, and/or confounding have been adequately excluded, and exposure to ETS is established as causally related to human lung cancer.

PROPERTIES

Environmental tobacco smoke (ETS) is the sum of sidestream smoke (SS) (interval between puffs), mainstream smoke (MS) emitted at the cigarette mothpiece during inhalation, compounds diffused through the wrapper, and MS that the smoker exhales (NRC 1986; U.S. EPA 1992; CEPA 1997). Tobacco pyrolysis products are formed both during smoke inhalation and during the interval between inhalations (NRC 1986). A number of chemicals present in ETS are known or suspected toxicants/irritants with various acute health effects. Prominent among them are the respiratory irritants: ammonia, formaldehyde, and sulfur dioxide. Acrolein, hydrogen cyanide, and formaldehyde affect mucociliary function and at higher concentrations can inhibit smoke clearance from lungs (Battista 1976). Nicotine is addictive and has several pharmacological and toxicological actions. Nitrogen oxides and phenol are some other toxicants present in ETS. Over 50 compounds in ETS have been identified as known or reasonably anticipated human carcinogens. Most of these compounds are present in the particulate phase (IARC 1986).

USE

There are no known uses of environmental tobacco smoke.

PRODUCTION

Environmental tobacco smoke is a direct result from lighting a cigarette and its production cannot be quantitatively measured.

EXPOSURE

Exposure to environmental tobacco smoke mainly results from inhalation of sidestream and exhaled mainstream smoke. The National Research Council (NRC) estimated that nonsmokers exposed to ETS averaged urinary concentrations of 25 ng/mL cotinine (active smokers had levels of 1,825 ng/mL). The cotinine level varies depending upon occupations, with higher cotinine concentrations for those occupations where workers are exposed to higher levels of tobacco smoke; such as in restaurants, bars and bowling alleys (Millar 1991). It should also be noted that many people who reported no exposure to ETS do have low levels of systemic cotinine, possibly from exposure to nicotine from the diet. Mean nicotine levels varied from 0.120 $\mu g/m^3$ to 21.5$\mu g/m^3$ depending upon various environmental exposure to ETS.

ETS exposure levels were also estimated by measuring respirable suspended particles (RSP) (<2.5 pm). Millar (1991) cited that Repace and Lowrey (1980, 1982) found RSP concentrations in public access buildings averaging 0.242 $\mu g/m^3$. In later studies, they estimated a 62% probability of nonsmoker exposure in the workplace. The mean RSP exposure levels varied from 18.5$\mu g/m^3$ to 45.4$\mu g/m^3$ depending upon the work environment (Repace and Lowrey 1980, 1982).

Levels of ETS in restaurants were found to be approximately 1.6-2.0 times higher than other office workplaces and 1.5 times higher than residences of, at least, one smoker. Isolating smokers to a specific section of restaurants was found to afford some protection for nonsmokers, but the best protection resulted from seating arrangements that segregated smokers by a wall or partition. Nonsmokers are still exposed to nicotine and respirable particles. Food-servers, who spend more time in restaurants, are exposed even more to ETS, though they may work in nonsmoking sections (Lambert *et al.*1993).

Levels of ETS in bars were found to be approximately 3.9-6.1 times higher than in office workplaces and 4.4-4.5 times higher than in residences. Bars are not always compelled to provide smoking and nonsmoking sections and this may account for the higher level of ETS exposure in bars versus restaurants (Siegel 1993).

Mattson *et al.* (1989) studied personal ETS exposure in airplanes. Levels of nicotine found in cabins seem to vary widely owing to unstandardized methods of collection and measurement. Oldaker and Conrad (1987) measured nicotine levels in the passenger cabins of commercial airliners. Using a hidden suitcase pump, they found that the average nicotine concentration in nonsmoking areas was 5.5 $\mu g/m^3$ (0.03-40.2 $\mu g/m^3$ [range, n=49]), while in the smoking sections it was 9.2 $\mu g/m^3$ (0.08-112.4 $\mu g/m^3$ [range, n=26]). Using these data, calculated "cigarette equivalents" for the smoking section ranged from 0.00008-0.15 cigarettes per 55 minute flight. Comparisons of the results, however, have shown some consistencies.

Studies have shown that nonsmoking seats near the smoking section have levels as high as those seats in smoking sections. The type of ventilation system a plane used seemed to be the most important factor in ETS exposure. Planes with 100% fresh air had lower levels of ETS compared to 50% fresh and 50% recirculating air. Recirculating air systems, however, have been used in more new planes because they improve fuel economy. Since attendants are not confined to the nonsmoking section, they had higher ETS exposures than passengers in nonsmoking sections (Mattson *et al.* 1989).

REGULATIONS

ETS is regulated by Environmental Protection Agency (EPA), food and Drug Administration (FDA), and Occupational Safety and Health Administration (OSHA). Regulations are summarized in Volume II, Table A-25.